Exploring Dynamics of Brain Volume Changes

1. Introduction

This report conducted the quantitative analysis using mixed-effects ANOVA including both within subjects and between subjects with a goal to explore how the dependent variables change over within-subjects factors and whether this change differs between between-subjects factors, accounting for the random effects of subjects. In addition, this report will conduct a statistical power analysis to understand the likelihood of detecting an effect if there is one.

The background and used dataset (INF2178_A4_data) comes from the Open Access Series of Imaging Studies (OASIS), which is a project aimed at making MRI datasets of the brain freely available to the scientific community. In this project, we will only use a few columns in this dataset by setting the variable *Visit* as the within-subjects factor and the variable *Group* as the between-subjects factor. Based on that, this report has conducted the mixed-effects of ANOVA in two directions.

1. **Direction 1:** How the clinical measures of eTIV(Estimated Total Intracranial Volume) change over visits, and does this change differ among groups classified by dementia status
2. **Direction 2:** Does nWBV (Normalized whole Brain Volume) exhibit different trajectories over time among subjects with different dementia statuses, and what are the implications for understanding the progression of cognitive decline

Before delving into the mixed-effects ANOVA, we first check if there are any missing values in any related columns, and we found that there are no missing values in the dataset except in the column of *SES* and *MMSE*, which is not related to our research question.

#1 Mixed-Effects ANOVA (eTIV as Dependent Variable)

The first mixed-effects ANOVA aims to understand the effect of two factors on the *eTIV*, where *Visit* is treated as a within-subjects factor and *Group* is a between-subjects factor. The *Subject ID* is used to identify individual subjects across visits. The following a brief summary of the final ANOVA table:

Group Effect **F-statistic:** 0.297 | **p-value:** 0.743

Visit Effect **F-statistic:** 0.225 | **p-value:** 0.003

Group-Visit Interaction **F-statistic:** 0.831 | **p-value:** 0.438

The p-value of 0.743 means that the F-test of the *Group* factor (between-subjects) is not statistically significant, indicating no significant differences in *eTIV* across different groups while the *Visit* factor shows a significant effect (p-value = 0.003) meaning that *eTIV* significantly changes over visits. Finally, the interaction between *Group* and *Visit* is not statistically significant (p-value = 0.438), suggesting that the change in *eTIV* over visits does not significantly differ across groups.

In summary, while the *eTIV* variable changes significantly within subjects across visits, this change does not differ significantly between different groups, nor is there a significant difference in *eTIV* across the groups when not considering the visit factor. Based on this finding, we stepped forwards to use pairwise comparisons to do the post hoc test, which can offer a more granular view following the formal ANOVA, helping to pinpoint where significant changes occur and affirming the main analysis findings. As a result, the post hoc test told us there is a significant change in *eTIV* across visits for the subjects, indicating that time or condition affects *eTIV* while there are no significant differences in *eTIV* were found between the groups, meaning the group factor does not significantly affect *eTIV*. Also the lack of significant differences in the interaction comparisons suggests that the effect of time or condition on *eTIV* does not differ across groups.

However, there are some challenges emerging in the assumptions check. When we conducted Mauchly's test for sphericity assumption and Shapiro-Wilk test for normality assumption, we found that the variances of the differences between all combinations of related groups are equal, which meets the sphericity assumption. On the other hand, the Shapiro-Wilk test results indicated that the distribution of the dependent variable at both levels of within-subjects factor

significantly deviates from normality, which violates the assumption of normality. Given these mixed results, our mixed-effects model may still remain a powerful alternative since mixed models can handle data that violate the assumptions of normality more flexibly by modeling individual subjects as random effects. Hence, the above findings of ANOVA may still have some useful insights.

#2 Mixed-Effects ANOVA (nWBV as Dependent Variable)

The second ANOVA provides insights into how *nWBV* is influenced by the same two factors before, as well as their interaction. The following is the brief summary of ANOVA table:

Group Effect **F-statistic:** 6.712 | **p-value:** 0.002

Visit Effect **F-statistic:** 94.251 | **p-value:** < 0.001

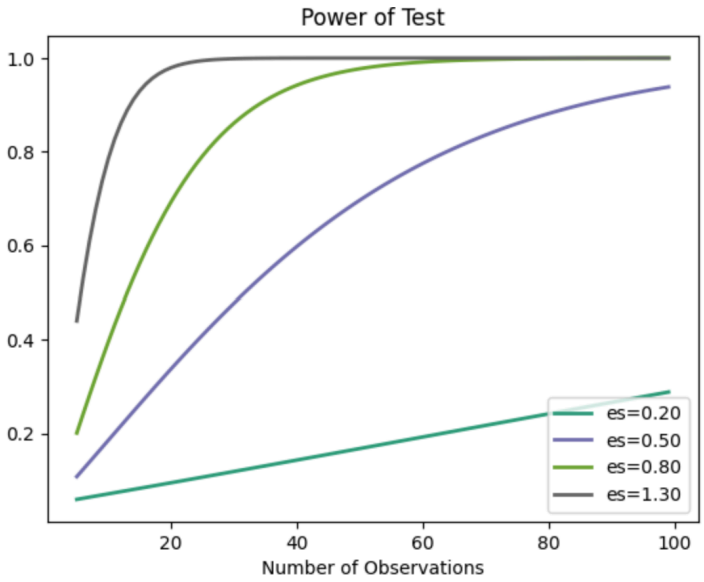
Group-Visit Interaction **F-statistic:** 1.534 | **p-value:** 0.219

Based on the result, both the group factor (p-value = 0.002) and the visit factor ($p<0.001$) have a significant effect on the level of nWBV. The partial eta squared suggests that around 8.7% of the total variance in nWBV is explained by the group membership. On the other hand, the statistics suggest that nWBV changes significantly over visits, accounting for 40.1% of the variances in nWBV, indicating a substantial within-subject effect. However, the interaction between group and visit is not statistically significant (p-value = 0.219), suggesting that the change in nWBV over visits does not significantly differ among the groups. Moreover, the post hoc test reinforced some findings like the significant change in nWBV and demented group showing a distinct pattern in nWBV compared to the nondemented group. However, the lack of significant differences between the converted group and other two groups in most comparisons suggests that the converted group's nWBV might not differ significantly from either demented or nondemented groups or that the sample size might be insufficient to detect such differences. Similar to previous ANOVA, we still check the assumptions of normality and sphericity. As the result, both the assumptions are met, indicating that the finding from ANOVA is effective and insightful.

Statistical Power Analysis

For the first power analysis, we have set the effect size, alpha value and desired power to find the sample size needed to achieve that power. Under the setting power of 0.8, we need a sample size of 64, rounded up from 63.7656. And then, we have conducted the power analysis by sketching

the power curve by varying effect size from 0.2 to 1.3 and different sample size, which gave the following graph:



Based on the graph, we can see some useful insights. First, for a given sample size, the power of the test increases with larger effect size, which means that it's easier to detect larger effects with smaller samples. Second, for any given effect size, increasing the sample size increases the power of the test. Lastly, researchers often aim for a power of 0.8 as a standard threshold, indicating a sufficiently low risk of Type II error. The graph shows how many observations are needed to achieve this power for different effect sizes. In conclusion, all these information could be a helpful tool for designing studies and understanding the balance between effect size, sample size, and the power of a test.

Conclusion

This research sought to explore the dynamics of brain volume changes, represented by eTIV and nWBV, over time and across different groups. Using a mixed-effects ANOVA, we examined these changes within individuals over multiple visits and between groups classified by dementia status. Both the ANOVA analysis revealed a significant change in nWBV and eTIV over time, irrespective of the group, which may support the hypothesis that brain volume is subject to change over time, potentially due to aging or disease progression.